

White. (J. Wm.)
and Wood. (H. C.)

IODIDE OF POTASSIUM IN SYPHILIS.

A DISCUSSION

BY

J. WILLIAM WHITE AND H. C. WOOD.

[REPRINTED FROM THE THERAPEUTIC GAZETTE FOR DECEMBER, 1888]

DETROIT, MICH.:
GEORGE S. DAVIS, PUBLISHER.
1888.

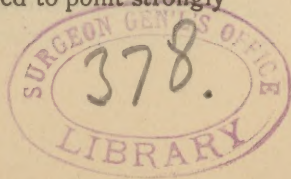


THE DIAGNOSTIC VALUE OF TOLERANCE OF THE IODIDES IN SYPHILIS.

BY J. WILLIAM WHITE, M.D.,

Clinical Professor of Genito-Urinary Surgery, University of Pennsylvania; Surgeon to the Philadelphia and German Hospitals, etc.

IN an able article upon syphilitic affections of the nerve-centres, Professor H. C. Wood, writing of cerebral syphilis, says, "In all cases of doubtful diagnosis the so-called therapeutic test should be employed, and if sixty grains of iodide of potassium per day fail to produce iodism, for all practical purposes the person may be considered to be a syphilitic." Jullien asserts that "the existence of syphilis contributes powerfully towards producing tolerance of the iodides. Experience proves, in fact, that in persons free from this poison the toxic phenomena of iodism are much more to be dreaded. In the same manner an antidote may be dangerous, or even fatal, when the organism is not under the influence of the poison which it is intended to combat." These statements, if well founded, convey an important practical lesson which is of the greatest value in the diagnosis of obscure conditions suspected to be of syphilitic origin. If unfounded, they may be seriously misleading. Dr. Wood contents himself with the simple statement of what he believes to be a clinical fact confirmed by his experience in large numbers of cases of disease of the nervous system. Jullien, in addition to appealing to experience, advances the theory that iodide-poisoning resembles the overaction of an antidote in the absence of the poison for which it is administered. He appears to think that this offers a satisfactory explanation of the circumstances. We have thus from the stand-point of a distinguished neurologist on the one hand, and an equally distinguished syphilographer on the other, an essential agreement in the statement that in doubtful cases the failure to produce iodism by large doses of the iodides may be considered to point strongly



towards the existence of syphilis. The question is certainly one in which every practical physician is interested ; if the above statements are correct, their truthfulness should be established beyond a doubt by the collective experience of the profession ; if incorrect, they are, as I have said, liable to be seriously misleading and dangerous. In examining, first, into the position of Dr. Wood, who bases his statement on his personal experience, it must not be forgotten that in weighing the probabilities of the case the negative evidence cannot be considered as nearly so strong as the affirmative. In other words, while every one would admit that the rapid disappearance of serious cerebral symptoms under the use of large doses of the iodides was strong presumptive evidence that the cause of these symptoms was syphilis, yet, on the other hand, if a similar case failed to respond to the same doses by an equally prompt disappearance of symptoms, it would not be safe to assume that, therefore, the disease is not specific.

If, however, in the latter case the large doses of iodides failed to produce the condition known as iodism, would it still be sound practice to base further treatment upon that fact, believing that, in spite of the persistence of the symptoms, the disease was probably specific ?

The term "iodism" should be understood to include the various forms of iodic intoxication, the most common of which are gastrointestinal irritation, coryza, lachrymation, mental depression, tinnitus aurium, and a pustular eruption (acne) upon the cutaneous surface of the body. While this pustular eruption is the most frequent exanthem produced by the iodides, it is true, as taught long ago by Ricord, that there is hardly any form of acute cutaneous eruption which they may not excite, erythema, eczema, and herpes being not uncommon. Bumstead (*American Journal of Medical Sciences*, p. 99, July, 1871) has described a case of pemphigus produced by the administration of the iodide of potassium, and states that Boinet quotes Cazenave as having seen a similar case. Since then Tilbury Fox, Duhring, Finny, Duckworth, Thin, and others, quoted by Dr. George F. Duffey (*The Dublin Journal of Medical Sciences*, April 1, 1880), in an article upon iodic purpura, have all recorded similar cases. Purpura, the most profound result of the influence of the iodide upon the skin, has been observed in a large number of cases, and has been very fully described in the article above mentioned. It seems probable that these various forms of skin-diseases are to be referred to the liberation of a less or greater quantity of free iodine in the tissues, although this has by no means been demonstrated. Binz (*Revue des Sciences Médicales*, tome v. p. 485) believes that, in the presence of the oxygen of the blood and the carbonic acid of the tissues, iodide of potassium is transformed into the bicarbonate of potassium with the liberation of free iodine. Kaemmerer describes this change as occurring in the blood and not in the tissues.

Various physiological and pathological theories have been advanced

to explain the cutaneous symptoms. Bogolopoff affirms that the iodide produces rapid dilatation of the peripheral vessels. Sée thought contraction of the arteries to be a symptom of iodine-poisoning. Hutchinson describes a variety which he believes to be due to thrombosis of the capillaries. Minich and others have referred these symptoms to fatty degeneration of the capillaries and to vaso-motor paralysis. Still others have attributed them to blood changes, producing a condition analogous to that of the blood in the purpura of scurvy, and associated with diminution of the amount of fibrin. The analyses of purpuric blood by Parks, Garrod, and others show, however, that in such blood the fibrin may be in excess. Nélaton believes that purpura is due to atony of the capillary system of blood-vessels, combined with abnormal fluidity of blood. Thin (*Medico-Chirurg. Transactions*, vol. lxii. p. 199, 1879) says that "the rationale of iodide eruption seems to be that there are conditions in which iodine when present in the blood attacks and disorganizes the blood-vessels at certain localized points. As a result of this injury to the wall of the vessel there is an escape of blood fluid into the surrounding tissue." He thinks that the papules of iodide acne, pemphigus, and purpura represent different degrees of involvement of the blood-vessels. The first is due to a limited œdema, with congestion; the second, to an effusion of serum, with more or less of the formed elements of the blood; the third, to destruction of the wall of the vessel and hemorrhage. Microscopical examinations in cases of death during the existence of iodide eruptions have seemed to confirm these observations. Duckworth has called attention to the relation of chronic nephritis to iodism, believing that when the elimination is reduced by kidney-disease the drug is maintained for a longer time in contact with the tissues. Fournier has recorded (*Revue Mensuelle de Méd. et de Chirurg.*, vol. i., 1877) fifteen cases of purpura from the use of the iodide in syphilitic subjects, the doses having been moderate, the patients in good average health, and showing no other hemorrhagic tendency. Dr. Duffey, in whose valuable paper many of the above references and a large number of others will be found, says that in the majority of cases of iodide of potassium eruptions that have been described the eruption appeared within a few days of taking the medicine, and in many cases after the use of but small doses of the iodide, and that it cannot, therefore, be maintained that any saturation of the system, either with iodine or the alkaline iodides, is necessary to produce iodism. Dr. Mackenzie has recorded a fatal case in a syphilitic child, following the administration of a single dose of $2\frac{1}{2}$ grains of iodide of potassium, and Ricord (quoted by Virchow and Duffey) is said to have observed purpura in a syphilitic subject whenever he administered iodide of potassium. He believes that there are certain idiosyncrasies which render the employment of iodide impossible, whatever may be the dose. Mr. Hutchinson long ago made the same statement, asserting that the production of iodide of potassium rashes depends far more

on the idiosyncrasies of the individual than on the dose administered. Dr. Henry Mead has recorded (*Dublin Journal of Medical Sciences*, p. 328, 1880) his experience, to the effect that the amount of the dose of iodide of potassium does not play an important part in regulating the poisonous effects of the drug, having seen such effects produced as frequently by very small doses as by large doses. Duffey says that about one-half of all the patients with iodic purpura of whom he had knowledge were syphilitic. Farquharson states that the only reason for the occurrence of many cases seems to be an individual peculiarity on the part of the patient, but that now and then a more plausible explanation may be given when we find cardiac or renal disease coinciding with the pustular rash of iodide of potassium. The citations already given serve sufficiently to show the variety of opinion which exists as to the essential cause of iodism, the weight of authority seeming to be in favor of the view of Dr. Thin, referring the skin-troubles at least to the effect upon the blood-vessels of free iodine. Whether this be correct or not, or whether the production of iodism is to be referred to some unknown quality of the tissues, our ignorance in regard to which we conceal under the name of idiosyncrasy, it is equally difficult to understand why the existence of syphilis, and particularly of late syphilis, should exert any preventive influence. Jullien's theory, which explains the alleged tolerance of large doses of iodide by syphilitic subjects through the presence of a poison, the destruction of which is supposed to exhaust the activity of the drug, can hardly be considered tenable. In a majority of syphilitic subjects the indications for the free use of iodine do not exist until the later or so-called tertiary stage, when the disease has lost all the peculiarities which indicate the presence in the blood and tissues of a living, active, generalized virus. Syphilis has then become non-symmetrical, non-contagious, and, in many cases, non-transmissible, and it is in the highest degree improbable that any virus exists in any form which would so neutralize the effect of the iodine or the iodides as by that means alone to prevent their action upon the healthy tissues. It is evident that if the theory in question—namely, that tolerance of large doses of the iodide is, other things being equal, symptomatic or indicative of the existence of syphilis—is to rest upon clinical evidence, the cases which support it, or which can be adduced as arguments either *pro* or *con*, must be very rare, and should include only those in which there has been opportunity for comparing in the same individual the action of full doses of iodides, before and after the contraction of syphilis. If the overwhelming and predominant influence of "idiosyncrasy" be admitted, the fallacy of assuming that special deductions as to the existence or non-existence of any disease may be drawn from the production or non-production of iodism becomes evident. The large majority of the cases of syphilis which come under the notice of the neurological specialists are in the later stages, and the difficulties of diagnosis are often extremely great.

While it is fair to assume that the rapid disappearance of coma, stupor, epilepsy, cranial pain, motor paralysis, and hemiplegia, under the influence of either large or small doses of the iodides, gives good presumptive evidence that the case is syphilitic, we can by no means assert that the persistence of those symptoms during the free use of iodides negatives the syphilitic theory of their origin. Seguin (*Archives of Medicine*, vol. xii. p. 128, 1885) has called attention to the fact that since Heubner has shown that very often in cerebral syphilis the lesion consists in obliteration of large arteries, with resulting ischæmia of a cerebral territory, and its death or softening, we must modify our prognosis and treatment. The moment that cerebral tissue undergoes such a process it is dead, and cannot be restored by any amount of iodide of potassium or of any other drug. The syphilitic lesion, in other words, may be amenable to treatment, while its residua are not. Now if, in such a case, iodide of potassium were administered without result, but with the production of iodism, after moderate or even large doses had been given, from the statements of Professors Wood and Jullien, we would be led to the conclusion that the case was non-specific, the failure to cure and the appearance of iodism both pointing in that direction. This might lead to the neglect of treatment of the greatest importance to the patient, for although it might not be possible to replace tissue already softened and disintegrated, further extension of the specific element of the disease process could readily be prevented. It might be possible to prolong life, even if entire health could not be restored. If, on the other hand, we are dealing with a case of chronic encephalitis or of apoplectic or embolic softening, due to other causes, but with a suspicion of syphilis, and if the patient's idiosyncrasy permits of the use of large doses of iodides without the production of iodism, we may be led by the above rule from a rational understanding and treatment of the case into an unwarranted dependence upon specific treatment. I have searched vainly through the literature of syphilis, and the records of the therapeutic and toxic action of the iodides, for any evidence corroborative of the above theory, but without much result. In the discussion elicited by Dr. Duffey's paper, Dr. Barton, of Dublin, said that it was well known that iodide of potassium acted in a different manner upon the syphilitic subject from what it did upon others, and that large doses were given to such patients for months without the production of any rash whatever, and I find a few similar statements indicating a moderately wide-spread existence of the same opinion, but, with the single exception of Jullien, I have not found it advanced by any syphilographer, the great majority of whom would doubtless agree with Mr. Hutchinson in the statements found in his last work on syphilis, one of the series of clinical manuals now in course of publication. He says (page 60), "The skin eruptions which may be produced by the iodides are very various in their characters; they are certainly due to idiosyncrasy, and have little or no relation to the

dose employed ;" and again (page 301), "The iodide of potassium is one of those remedies of which it is curiously true that in many persons the dose makes little or no difference in its effects ; one grain may produce iodism in some, while one drachm will not in others." "There is, perhaps, no drug in which the influence of idiosyncrasy comes more frequently or more permanently into play. To some patients even very small doses are poisonous, while a large majority can take indefinitely large ones with impunity."

In investigating this subject I have carefully gone over my case-books for the past ten years, in the search for cases the circumstances of which rendered them of value in the present argument. I have found but three which complied with all the necessary conditions, which, as it seems to me, must include an observation as to the effect of iodide upon the same individual before and after the acquirement of syphilis ; and, moreover, the effect of the same drug during the existence of undoubted syphilitic symptoms.

These cases may be summarized as follows :

CASE I.—A. B., a medical student, aged 19, consulted me in 1877 for an ordinary case of gonorrhœa. During its course he developed a severe urethral synovitis, affecting the knee- and wrist-joints. He was treated by me after the method which I then employed, and which included the free use of the iodides. My case-book shows that, failing to produce relief with smaller doses, the drug was administered for a few days in quantities reaching from two drachms to three drachms daily, and for a much longer period in doses only a very little smaller. There were no symptoms of iodism whatever. This gentleman graduated, leaving Philadelphia to engage in the practice of medicine in a small town in Pennsylvania, and I heard no more of him for some years. He reappeared in my office in 1882, with tertiary syphilis, the manifestations of which at that time were rupial sores upon both upper and lower extremities and upon the lower portion of the back, with ulceration of the mucous membrane covering the hard palate and of the walls of the pharynx. He told me that he had reached this condition through no wilful neglect on his own part, but that in his frequent attempts at specific treatment he had invariably found that even small doses (5 grains three or four times daily) of the iodide of potassium would produce the most unpleasant symptoms.

Disregarding this statement, I prescribed for him a course of mixed treatment and kept him under observation. I found that the susceptibility which he described undoubtedly existed, and that after taking the iodide for a few days his condition was really distressing, the coryza and the gastro-intestinal symptoms being particularly annoying. I finally cured him through the alternate administration of the mixed treatment and the *Succus Alterans* (McDade's formula).

CASE II.—A young man who had recently had gonorrhœal epididymitis applied to me in 1878, on account of the usual induration which

remained, and which, being of an exceptional size, gave rise to considerable mental anxiety. I prescribed inunctions and iodide of potassium internally, running up the dose of the latter to 10 grains, four to six times daily. No effect upon the induration was produced, and there were no symptoms of iodism whatever. In 1884 the same patient returned with evidences of syphilis, in the shape of periosteal nodes, ulcerating mucous patches about the scrotum and anus, and a very large progressive and ugly-looking ulcer situated over the spine of the left tibia. On account of this latter symptom I put him to bed in a private room in the University Hospital and placed him on the mixed treatment; but found he could take barely one-third the dose he had formerly taken, and that even this amount (5 grains four times daily) produced pustular acne with a strong tendency to the formation of actual furuncles. Before he recovered entirely I was compelled several times to intermit the use of the iodide, and to give short courses of Fowler's solution.

CASE III.—This case has occurred in my practice since I began to think of the subject of this paper. It does not precisely meet all the requirements, but is, I think, valuable as showing not only the permanent influence of personal idiosyncrasy in the production of iodism, but also that even in the presence of active syphilis this susceptibility may vary in the same individual from time to time.

A merchant doing business in the northern portion of Pennsylvania came to me a year or two ago with a syphilitic ecthyma widely distributed, and with a tubercular syphiloderm of the side of the nose and cheek. He did very well under the ordinary mixed treatment, returned home free from all symptoms of the disease, and after writing to me two or three letters, to all of which I replied recommending the continuance of the treatment, he ceased to communicate with me. A few weeks ago he reappeared in my office, having been brought there by a friend in a truly pitiable condition. He had been suddenly stricken with right-sided hemiplegia while talking through a telephone a short time previously, and was only just recovering sufficiently to hobble unsteadily around. He had marked aphasia, and was quite unable to express himself intelligibly or to understand what was said to him unless the speaker was extremely slow and deliberate. I placed him immediately upon mercurial inunctions, and ordered 10 grains of iodide of potassium in combination with the syrup and fluid extract of sarsaparilla four times daily, increasing it within a few days to six times daily. There was a rapid amelioration of his nervous symptoms, so that after two weeks' treatment he walked with no difficulty and talked with much greater fluency, but at the same time he suffered from an outbreak of iodide acne which was very marked and annoying. This persisted in spite of the combination of Fowler's solution with the treatment, and was associated with marked coryza. As, however, he seemed to digest the medicine well, and as his nervous symptoms had

been so serious and threatening, I continued to push the iodide in spite of the eruptions which it produced. He had two or three severe furuncles, tinnitus aurium, and finally began to have, under doses of 20 grains four times daily, considerable diarrhœa, so that I was finally compelled to intermit the use of the drug. He has since made further improvement under the alternate use of the mixed treatment and Succus Alterans. The diuretic and alterative properties of the latter make it of value occasionally as an adjuvant, especially in patients with intolerance of the iodides, or in the rarer instances where mercurials persistently cause trouble.

These cases, while altogether insufficient to generalize from, seem to me interesting examples of the fact that there is some other element than the existence of syphilis in any stage which determines the production or non-production of iodism, and when taken in conjunction with the absence of satisfactory evidence in the opposite direction, appear to justify the following conclusions :

1. Personal idiosyncrasy is so strong a factor in relation to the toxic symptoms produced by the iodides, that it quite overshadows any possible influence due to the existence of syphilis.

2. There are no satisfactory theoretical grounds for believing that syphilis in any stage prevents the production of iodism by a process of neutralization, and this is particularly unlikely to be true as regards the latter stages.

3. It is, therefore, most unsafe to base any diagnostic conclusion upon the presence or absence of toxic symptoms (iodism) after the administration of full doses of the iodides.

THE IODIDE OF POTASSIUM IN SYPHILIS.

BY H. C. WOOD, M.D.

THE question raised by Professor White is one of such great practical importance that the editors of the THERAPEUTIC GAZETTE have adopted the unusual course of handing Dr. White's article to me, in order that both sides of the question may be heard in the same journal, I consenting that Dr. White should close the discussion.

In the first place, it is essential to the proper understanding of the subject that we separate fact from theory, and consider the question, Does iodide of potassium have any relation with syphilis? entirely apart from the query, How do the iodides act in syphilis?

I shall not occupy much space with the discussion of the theory of the subject; we have too little positive knowledge of the method in which syphilis affects the system, and of the way in which the iodides act upon the organism, to allow our speculations upon such points to be of much value. We only know that there is a poison introduced by syphilitic infection which so profoundly influences the organism as to affect all of its tissues, and that the iodide of potassium also has the power of profoundly altering the general nutrition of the body. I believe that the actions of the two poisons are in some way antagonistically related; but this antagonism is not necessarily direct. It is not, to my thinking, probable that the drug directly antagonizes the syphilitic virus; it is more likely that the virus produces in the system changes, which secondary changes in turn alter the relation of the organism to the iodides. I do not believe in the existence of any direct antagonism between the two poisons, such as exists between an acid and an alkali, or even between two drugs which are physiologically opposed to one another, such as opium and atropine, or digitalis and aconite.

Passing by the theory of the subject as comparatively unimportant, we come to the vital clinical question.

At this point I must disagree with Dr. White as to the method of obtaining satisfactory evidence concerning the relations of the iodide with syphilis. I do not believe the question can ever be satisfactorily answered by studying individual patients before and after the acquiring

of syphilis ; especially, must trustworthy cases of such character be most infrequent, because the tolerance of the iodide is probably a late phenomenon of syphilis, so that for our purpose it would be necessary to compare an individual with himself as he was eight, ten, or twelve years previously. The fewness of such opportunities would make it practically impossible to eliminate "the overwhelming and predominant influence of idiosyncrasy."

Taking the cases narrated by Dr. White himself, I find that in the first the patient was suffering from gonorrhœal rheumatism when he took the iodide for the first time. I do not know how far the virus of gonorrhœal rheumatism is antagonistic to the iodide, but it is not established that no antagonism exists between the two poisons. The comparison made by Dr. White is in this instance not between the normal individual and the same individual after the contraction of the syphilis, but between the individual when under the influence of the virus of gonorrhœal rheumatism and the same individual under the influence of the syphilitic poison. In case second, the young man apparently had an "idiosyncrasy" towards the iodide of potassium, since the normal average adult certainly cannot bear sixty grains of iodide of potassium a day ; and we cannot with propriety reason from cases which present idiosyncrasy to the average individual. The third case is simply an instance of a man who, in spite of being syphilitic, could only bear moderate doses of the iodide. The value of these cases seems to me very little.

I must also disagree with Dr. White in regard to arguments drawn from cases other than those in which the iodide has been given before and after the occurrence of the syphilis. Suppose, for example, it is found that out of a thousand cases of a disease which we will call A, nine hundred and ninety-five bear well enormous doses of a remedy which cannot be given at all to any five out of every thousand normal individuals ; certainly this would prove that the disease A has a distinct antagonistic relation to the remedy. It is a parallel line of reasoning to this which has led me to the views which I hold in regard to the iodide of potassium. Unfortunately, owing to the loose methods in which most American hospitals keep their records, it is impossible for me to make a tabulated statement of cases ; but under the circumstances I think I may, without being open to the criticism of egotism, indicate the extent of the experience from which is drawn the positive opinions which I hold upon the subject.

As neurologist to the University Hospital I have under my care all the nervous patients in the wards and the dispensary. I am officially notified by the clerk of the hospital that there have been treated up to the first of the present year six hundred and ninety-six cases in the hospital and four thousand one hundred and ninety-eight cases in the dispensary. Of over five thousand cases which have thus been under my care, at least fifteen per cent., or seven hundred and fifty cases, have

been in the persons of syphilitics. In the Philadelphia Hospital, according to the best estimate based upon official figures that Dr. C. K. Mills and myself have been able to make, there have been, during the seventeen years of my service, under my care somewhat over two thousand patients suffering from disease of the nervous system, of which more than fifty per cent.—and according to my thinking seventy-five per cent.—have suffered from syphilis. If to these cases be added those which I have come in contact with in private practice and as consultant to public and private hospitals for the insane, I think that I may claim to have seen nearly two thousand cases of nervous disease in the persons of syphilitics.

This experience has demonstrated to me—as a proposition whose truth is established—that in nerve syphilis there is usually an extraordinary tolerance of the iodide, so that almost all such syphilitic subjects will bear doses of 20 grains and over frequently repeated ; it is, indeed, true that there are a few persons who are suffering from undoubted syphilis but in whom this tolerance does not exist, but such patients are exceptional. There are a very few healthy persons who can take the iodide at once in large doses without any serious inconvenience, and there is a still more numerous class in whom tolerance of the iodide can be established by commencing with smaller doses and gradually increasing the dose. The vast majority, however, of persons who are free from syphilitic affection, cannot take doses of over 10 grains of the iodide three times a day without the production of iodism, unless as the result of the habitual use of the remedy. When iodides are tolerated by the normal individual, such individual is said to have an idiosyncrasy, which makes him an exception to the general rule. In syphilitics this rule is reversed, and when the person suffering from syphilis cannot endure iodides the lack of tolerance is owing to an idiosyncrasy,—*i.e.*, the individual is an exception to the general rule. The number of exceptions to the rule in either case is so small that, for the purposes of practical medicine, when we find that a person can tolerate large doses of the iodides, the probabilities that such person is suffering from syphilitic infection are so strong as to warrant the diagnosis of syphilis if the tolerance of the iodide is accompanied by the presence of symptoms of organic disease not readily explainable.

I have no doubt that Dr. White has had a large experience in syphilitic disease, and have great respect for his powers of observation and his judgment ; why, then, have we reached such different conclusions ? I might here well argue as a defence that numerous authorities can be quoted as asserting that in all stages of syphilis mercury is injurious ; whereas the large majority of the profession believe that mercury is of great value in the treatment of syphilis. I do not think, however, that such a line of argument is necessary in this case. It so happens that the experience of Dr. White has been chiefly with patients who suffer from the earlier stages of the disorder ; while my

experience, so far as regards the use of iodide of potassium, has been almost solely with persons in the advanced stages of the disease. In the comparatively few cases of primary and early secondary syphilis which I have had to treat, I have found that a very considerable proportion of the patients will not bear the use of the iodides, and I believe that the *tolerance of the iodides* belongs to the *advanced* rather than the *early stages* of the disorder.

The converse of the opinion which was stated a few lines back does not hold with as much force upon the practitioner as does the proposition itself. The production of iodism by small doses of the drug is, however, evidence (not proof) that the patient is not suffering from syphilitic disorder, and in any given case renders it probable that the symptoms are not the result of syphilitic affection. It is, however, in practice essential to remember that there are exceptions to the general rule, and that whenever there is a clear history of infection, and the symptoms trend towards specific disease, trials of other forms of anti-specific medication should be made before the final working opinion is formed. Thus, last spring, I saw a gentleman from a distant city in whom in middle life epileptic convulsions had developed with mental failure, evidences of ocular paralysis, headache, and great depression of the general health, and in whom there was a clear history of chancre. He would not tolerate iodide of potassium at all; even small doses caused great gastric disturbance. The careful use of mercurials followed by the employment of the iodide in very small doses has restored this patient to health. I mention this case here not merely illustrating the exception to the general rule, but as illustrating a very important fact,—namely, that in some of these instances the iodide is not devoid of control over the specific disease, but is only in relation to the individual patient excessively active, 4, 5, or 6 grains affecting the general system as much as 50 or 60 grains commonly do in such cases; so that a cure may sometimes be obtained by reducing the dose to so small a quantity that no iodic irritation is caused.

At one time it was my habit to give a very favorable prognosis in any individual case so soon as I was sure of the tolerance of the iodide. I now know that it is possible for a syphilitic patient to tolerate the iodides in indefinite doses and yet to obtain no relief from their use. A favorable prognosis ought not, therefore, to be based upon the simple tolerance of the drug; but when along with such tolerance the symptoms soon begin to rapidly ameliorate, there is always good grounds for predicting a more or less complete recovery.

Even under the most hopeful circumstances, however, we are liable to be cruelly disappointed, so that, although encouragement should be given and the probabilities of recovery be stated, at least to the friends of the patient we should express the possibilities of an unsuspected disaster.

The causes why the iodides may be tolerated by the syphilitic person,

suffering from organic nervous disease, and yet afford no relief are several.

In the *first place*, there is a class of cases in which the primary lesion is in the blood-vessels, and we have no sufficient ground for believing that a syphilitic atheroma, which is at all advanced, is capable of being cured by treatment; but I confess that my experience leads me to doubt the frequency of cases in which severe syphilitic atheroma of the brain-vessels exists without general atheroma of the arterial system, or gummatous or sclerotic disease of the brain.

In the *second place*, I have seen very numerous cases in which either sclerosis of the nerve-centres or the lesions of dementia paralytica have been present in syphilitic persons, who have had a tolerance of the iodides but have not been benefited by their use.

The discussion of the connection between sclerosis of the nerve-centres and syphilis would lead too far from the present subject to be entered into here. Suffice it to say that I am well convinced that there is a relation between the two affections; but whether the syphilis acts directly or indirectly is a matter which cannot at present be settled. The important practical fact is that sclerosis occurring in syphilitic subjects is not amenable to antisiphilitic treatment. The same is true of the lesions of dementia paralytica. Certain forms of syphilitic disease of the cerebral cortex produce symptoms which so closely resemble those of dementia paralytica, that I do not think it is always possible to separate the two sets of cases diagnostically, except as the result of therapeutic trial. Clauston, I believe, asserts that we have no right to make the diagnosis of dementia paralytica until the period of development of physical symptoms is reached. As the affection occurs in this country, however, I am sure that if we wait until this stage we will wait until the diagnosis is of very little value. As illustrating this point, and also the relations of the disease to relievable syphilitic brain affection, I may mention the case of a gentleman who came under my care two years ago. There were no pronounced delusions of grandeur, but the man had been buying real estate in enormous quantities, and had also been extending his business, to the alarm of his partners. Some time after my diagnosis was made it was discovered that his intent in buying the real estate had been to make an enormous hotel, in which the poor widows of his city should live without charge. His case was brought to a crisis by his making indecent assaults on two or three women, and being arrested by the police. There was a clear history of syphilis, and I gave at once a positive opinion that the patient was suffering from either dementia paralytica or cerebral syphilis. As there were no ocular symptoms, and no failure of physical force, my opinion was based upon the change of character in the patient, his excessive high spirits, his sexual excitement, and the outrageous outcomes which it had led to, taken along with the slight evidences of mental failure, which became evident to me on talking with him. There had been no paralysis, no fits,

and no headache, so that the diagnosis inclined rather to dementia paralytica than to true syphilis. On the other hand, there was not only the lack of weakness, but an absolute exaltation of physical power. The man, who had been simply a quiet gentleman of sedentary habits, had become a restless, excited pedestrian, who, after a walk of fifteen miles at the highest speed, was still fresh although his professional attendant was exhausted. Iodides in the largest doses produced no signs of iodism, and our hopes of relief were excited; but in spite of anti-specific treatment the case went steadily onward. Loss of physical power did not, however, manifest itself until after the mental degradation had become so great that the patient could not join six words coherently. Epileptic convulsions came on, and, although the physical weakness never approached paralysis, death occurred in a fit. The ordinary lesions of dementia paralytica were revealed at the post-mortem.

In the *third place*, a gummatous tumor may itself be entirely subordinate to the iodides, and yet have set up by pressure a lesion of the surrounding nerve-centre which is not controllable by any specific medication, so that symptoms of organic brain-disease may continue after the removal of the gumma. A case in which I had an opportunity to make the autopsy illustrates this point well. In a man who had long suffered from cerebral syphilis, under the influence of the large doses of the iodides and of the mercurials the symptoms had all disappeared, except that at irregular intervals epileptic convulsions recurred, and were not controlled by long-continued and very careful specific medication. In one of these convulsions the man died, and, after death, in the cerebral cortex a small patch of sclerosis was discovered, evidently a scar, marking the former site of a gumma. In such a case as this surgical interference might be called for, provided the exact site of the lesion could be located, but it is only in such a case that surgical interference is warranted in syphilis; so long as there is reason to believe that there is a cerebral gumma, so long should the surgeon's knife be kept away. Even, however, when the lesion in the syphilitic brain has been reduced to a sclerosis, which is the scar of the original disease, it is by no means positive that the surgeon can do permanent good. Temporary relief may be very well afforded in such a case by cutting out the diseased tissue, but by and by in all probability the scar produced by the surgeon's knife will itself take on the sclerotic changes, and a return of the original symptoms mark the recurrence of the lesion. In other words, the danger is that a medical scar shall be simply substituted by a surgical scar. These considerations apply not only to syphilitic cases but to various brain-diseases, and it is very probable that operation will fail to be of permanent service in idiopathic and other epilepsies, even when the neurologist can locate the portion of the brain at which the discharge of convulsive force begins.

In any individual case of cerebral syphilis the first therapeutic question which must be decided by the practitioner is usually as to whether mercurials or the iodides should be employed; and as experience has led me to modify the original views which I held upon this matter, the discussion of the subject may not lack interest. As a medical student, I was taught that the iodides of potassium are suitable for the treatment of advanced syphilis, while the mercurials should be chiefly reserved to combat the early manifestation of the disorder. There is a certain amount of truth in this distinction, but what truth there is applies not so much to cases of cerebral syphilis as to other forms of the advanced disease. Cerebral gummata may, of course, develop when disease of the bone and other deep tissues shows a wide-spread general infection, which is also manifested by the failure of vitality; but in the great majority of cases of cerebral syphilis that have come under my care, especially in private practice, there have been no pronounced wide-spread lesions, no breaking down of tissue, and no cachexia.

To my thinking, the decision, whether iodide or mercurials should be employed, ought to rest upon the symptoms of the individual case rather than upon the stage of the disorder. The contraindication for the free use of mercurials is not the number of years since the primary affection, but a condition of low vitality and a tendency to necrotic changes. Under these circumstances, mercurials, if employed at all, must be used with the greatest caution. In a few cases, however, I have obtained the best results by withdrawing the ordinary mercurials and iodides, and giving large doses of tincture of iron, with small doses of corrosive sublimate, although there was a distinct cachexia. The following prescription affords a mixture whose taste is usually not objected to, and which in most cases agrees with the stomach. The dose of it, and, indeed, the proportion of the ingredients, should be varied to suit individual cases.

R Hydrarg. chl. corrosiv., gr. iss ;
 Tr. ferri chlorid., fʒii ;
 Glycerinæ, fʒi ;
 Ol. caryophylli, ℥xviii ;
 Syrupi, q. s. ad fʒxviii. M.
 S.—Teaspoonful after meals.

A very great disadvantage attends the use of the iodides,—namely, the slowness of their action. In some cases this is a matter of minor importance, but in other instances it is vital. There occur to my thinking at this moment two cases which have been under my care in which the iodides were being used freely, and in which the symptoms had greatly ameliorated, although occasional epileptic convulsions still occurred. In each case the respiratory arrest of an epileptic fit lasted a moment too long, and death resulted. At the autopsy gummatous lesions were found which were evidently yielding to the iodide of potas-

sium. The iodide would probably have sufficed for the cure had it not been for the fatal accident of the long arrest of respiration; but if mercury had been exhibited so soon as the cases came under my care the rapid removal of the lesions would have probably prevented the fatal fit. More and more has it come to be with me a favorite rule of action in cerebral syphilis without evidences of cachexia or a distinct history of mercurialization to begin the treatment with mercury in such doses as are necessary to cause slight salivation, and to maintain this impression for some days or weeks *pro re nata*.

After pytalism, either in syphilitic or nonsyphilitic subject, a course of iodide of potassium should be given so as to secure elimination of the mercury from the system. When in a case of cerebral syphilis the time for the exhibition of the iodide has arrived, the question of the dose becomes important. It is usually best to begin with 10 grains three times a day; in the course of two or three days this dose may be increased to 20 grains three times a day. Usually the patient who will tolerate a drachm of iodide a day will tolerate two drachms a day. A majority of those persons who can take two drachms a day without the production of iodism can take three drachms. It is, therefore, safe to advance the dose very rapidly after it has been found that a drachm a day causes no inconvenience. Not rarely it seems almost impossible to produce iodism. I have frequently given the iodides up to or even beyond six drachms a day. I do not believe that larger amounts than these are of any especial service, and I am not sure that any advantage is gained by going beyond a daily dose of half an ounce. Although the iodide is known to pass readily through animal membranes, the suggestion naturally presents itself that probably much of such a dose as this fails of absorption. In order to test this question, I recently had a quantitative analysis made by Dr. John Marshall, Demonstrator of Chemistry in the Medical Department of the University of Pennsylvania, of the urine of a patient who was taking three hundred and sixty grains of the iodide a day. The results are as follows:

First twenty-four hours,—total quantity of urine passed 1253 c.c.; potassium iodide, 16.84 grammes (258 grains).

Second twenty-four hours,—total quantity of urine passed 1621 c.c.; potassium iodide, 20.2 grammes (310 grains).

Third twenty-four hours,—total quantity of urine passed 1531 c.c.; potassium iodide, 17.606 grammes (270 grains).

Fourth twenty-four hours,—total quantity of urine passed 1078 c.c.; potassium iodide, 14.488 grammes (222 grains).

The average daily amount of the iodide recovered from the urine by Dr. Marshall was two hundred and sixty-five grains against three hundred and sixty grains ingested. It is almost certain that the iodide when given in large amount is freely eliminated by the intestines, as well as in the saliva and perspiration, and I think the reader, making a proper allowance for such loss, will agree with me that the work of Dr. Marshall

shows that the iodide, when given in daily doses of three hundred and sixty grains, is practically all absorbed.

Whenever symptoms of iodism are apparent in cases of cerebral syphilis, the remedy should be withdrawn for a few days, and then smaller doses administered, the effort being to keep just within the line of iodide intoxication. Owing to the necessity for frequent varying of the dose, it is preferable to exhibit the iodide in solution by itself, and adding in the vehicle used to cover the taste of the iodide at the time of administration.

The iodide is so soluble that a watery solution, one minim of which represents a grain of the salt, is readily made, and is permanent. I have been accustomed to use the following formula, directing the patient to add to a dessert- or tablespoonful of No. 2 and a quarter tumbler of water the desired number of minims of No. 1 :

℞ Potassii iodidi, ℥i;
Aquæ, q. s. ad f℥ii.
S.—No. 1.

℞ Syr. sarsaparillæ comp., f℥viii.
S.—No. 2.

At one time the profession had a great deal of confidence in the value of the so-called "Woods" in advanced syphilis; at present they are very little used, yet I am not sure that they possess no value. At present writing one case recurs to my mind in which a long treatment with the ordinary forms of mercurials and iodides had entirely failed to achieve good; but in which "Zittmann's Decoction" was exhibited with rapid results.

The compound syrup of sarsaparilla is too feeble in medicinal ingredients, and too active in sugar, to have any other value save as a vehicle which shall cover the taste of the iodide; but if the compound fluid extract of sarsaparilla be added to the prescription No. 2, so that the patient gets a dessertspoonful in each teaspoonful, a very fair imitation of the older preparations of the "Woods" will be had.

IODISM AND SYPHILIS.

I HAVE read with great interest Professor Wood's criticism of the paper which I placed in his hands for publication, and desire, with his kind permission, to make the following brief statements in reply thereto :

1. Professor Wood, in disagreeing with me as to the character of the evidence required in the present discussion, materially enlarges its limits by stating it as "the relation of the iodides to syphilis." That is a very broad question upon which I have decided views, but into which I did not enter. It is, as the title of my paper indicates, the relation of *iodism* to syphilis which I desired to discuss, and so much of Professor Wood's reply as goes into the larger field is, therefore, somewhat irrelevant, though I may add that it constitutes an interesting contribution to the literature of the subject.

2. While Professor Wood and I agree as to the great rarity of cases which bear directly upon the question, it seems to me that that fact, as stated by him, strongly fortifies my position,—*i.e.*, that the "fewness of opportunities" for observing individuals under the influence of iodide, both before and after the development of late syphilis, makes it "practically impossible" to eliminate the element of idiosyncrasy. If this is true, and I agree with Dr. Wood in believing it to be so, and if Mr. Hutchinson is right in asserting, after his enormous experience with all forms and stages of syphilis, that the skin eruptions produced by the iodides are certainly due to idiosyncrasy and have little or no relation to the dose employed, then my conclusion as to the valuelessness of iodism (or of its absence) as a diagnostic factor is sustained rather than weakened.

3. As to the cases I have given : Gonorrhœal rheumatism (or urethral synovitis), which was present in Case I., is generally thought to be a septicæmic manifestation not dependent upon any specific virus ; but for the sake of argument the possible existence of such a poison may be admitted. Dr. Wood rejects the case on account of an hypothetical antagonism between the remedy and the virus, which prevented the production of iodism. But if gonorrhœal rheumatism may do this, why may not many other diseases do likewise? And if so, how can it be safe to say in any given case that it is syphilis and not one of the other maladies which is preventing iodism? If the case is declared valueless on that theory, the absence of iodism certainly ceases to assume

any definite relation to the existence of syphilis, the view which I am trying to maintain by another line of argument.

In criticising Case II. Dr. Wood simply restates my position. My patient undoubtedly had an "idiosyncrasy" which enabled him to take very large doses of iodide with impunity. Suppose now that he had suffered from obscure nervous trouble, simulating syphilis. Would the absence of iodism have warranted a diagnosis of syphilis, or even have pointed strongly in that direction? I think not.

Case III. certainly shows that an individual with late nervous syphilis may have toxic symptoms after small doses of iodide. Suppose in this instance that I had been in doubt as to the character of his hemiplegic attack. Would it have been safe to argue that if its cause had been syphilis there would have been tolerance of the iodide, and that therefore it would be well to search for some other etiological factor? I think not, and yet that would have been entirely logical if the views which I am opposing were correct.

The cases still seem to me pertinent to the discussion and of distinct value.

4. If there were even approximate parallelism between Dr. Wood's suppositious case (of a disease "A" and its remedy) and the facts as to syphilis and the iodides, further argument would be useless and Dr. Wood's position would be established. That this is not the case, or at least that it is quite unproven, I have tried to show in my paper.

5. In conclusion, I must respectfully protest against the assumption that there is any material difference between the sum total of my experience with late syphilis and that of Dr. Wood. For years I have been seeing patients in all stages of syphilis and of suspected syphilis; not, of course, with nervous symptoms exclusively, but with them as well as with all others. If Dr. Wood means that the tolerance of iodides is a phenomenon peculiar to nervous syphilis, I must admit his greater experience. Otherwise, I should feel obliged to claim at least equal weight in the argument for my statements in regard to late as well as to early syphilis. It should be remembered also that, in common with the great majority of syphilographers, I give the iodide of potassium in the early stages of the disease only in exceptional cases. When any recognized authority speaks of the relation of the iodides to syphilis, it is safe to assume that, like Dr. Wood, he refers to syphilis in its later stages.

I would be thankful for the existence of such a diagnostic rule as is formulated by Dr. Wood; but I think I have tested it thoroughly, and, basing my views both on the theoretical considerations which I have advanced and on my clinical experience, I cannot, even after reading Dr. Wood's very able paper, see any reason for changing my opinion.

J. WILLIAM WHITE.

1810 S. RITTENHOUSE SQUARE, PHILADELPHIA.

